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None

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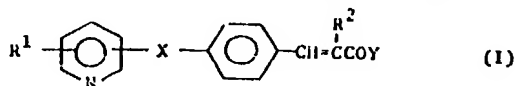
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(54) Pyridyl oxy- or thio-phenyl pharmaceutical compounds

(57) Pyridyl compounds are represented by the general formula



where X is -O- or -S-, R<sup>1</sup> and R<sup>2</sup> each is H or C1-3 alkyl, Y is -OH, -OR<sup>3</sup> or -NR<sup>4</sup>R<sup>5</sup> where R<sup>3</sup> is C1-4 alkyl and R<sup>4</sup> and R<sup>5</sup> each are H or C1-4 alkyl or C3-6 cycloalkyl. Pharmaceutically acceptable salts include acid addition salts and metal salts of the carboxyl group.

Four preparations are described, according to the nature of Y.

Pharmaceutical compositions contains the compounds for dosage of 0.1 to 60 mg/kg body weight orally or 0.01 to 4 mg/kg by injection.

The compounds have specific inhibitory activity on thromboxane A<sub>2</sub> biosynthesis and are useful for prevention and treatment of disorders caused by thromboxane A<sub>2</sub>, such as thrombosis or cardiac infarction.

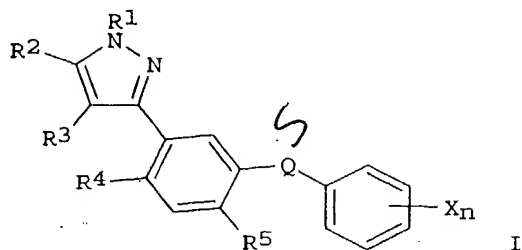
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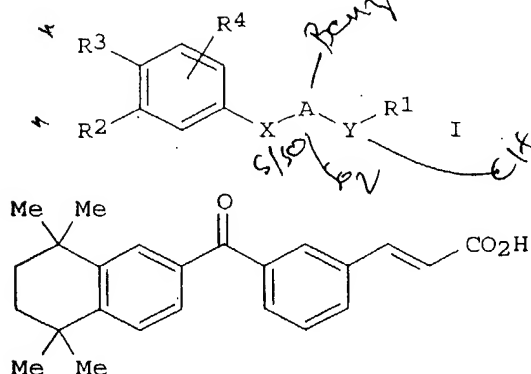
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AB Title compds. [I; n = 0-5; Q = O, S, SO, SO<sub>2</sub>, imino; R<sub>1</sub> = H, (substituted) alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl; R<sub>2</sub> = (substituted) alkyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonylalkenyl, alkenyloxy, alkenylthio, alkynyl, alkynyloxy, alkynylthio, cycloalkyl, cycloalkylalkyl; R<sub>3</sub> = H, halo, (substituted) alkyl; R<sub>4</sub> = H, cyano, thiocarbamoyl, halo; R<sub>5</sub> = cyano, thiocarbamoyl, halo, (substituted) alkyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl; X = OH, amino, NO<sub>2</sub>, cyano, CO<sub>2</sub>H, carbamoyl, thiocarbamoyl, F, Cl, Br, iodo, (substituted) alkyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, etc.], were prepared Thus, Et 2-(4-hydroxyphenoxy)propionate in Me<sub>2</sub>SO was treated with NaH and then with 4-bromo-3-(4-cyano-2,5-difluorophenyl)-5-difluoromethoxy-1-methyl-1H-pyrazole followed by 2.5 h stirring to give 56% Et 2-[4-[2-cyano-5-[4-bromo-5-(difluoromethoxy)-1-methyl-1H-pyrazol-3-yl]-4-fluorophenoxy]phenoxy]propionate. The latter showed strong herbicidal activity and was well tolerated by crop plants.



II

AB The invention concerns novel bi-aromatic compds. I [R1 = Me, CH2OR5, OR5, COR6; Y = (un)substituted CH:CH or C.tplbond.C; A = (un)substituted divalent (ortho or meta) benzene, furan, thiophene, or pyridine nucleus; X = O, S, SO, SO2, CO, C(:CH2), C(:CMe2), CH2, etc.; R2, R3 = H, alkyl, OR5, SR5, polyether; or R2R3 may form ring optionally substituted by Me or interrupted by O or S; R4 = H, halo, alkyl, OR5, polyether; R5 = H, alkyl, acyl; R6 = H, alkyl, (un)substituted NH2 or OH]. The compds. are agonists or antagonists of RXR receptors (no data), and can be used in pharmaceutical compns. for human or veterinary medicine (in particular for treating dermatol., rheumatic, respiratory, cardiovascular, and ophthalmol. disorders), as well as cosmetic compns. For instance, Friedel-Crafts acylation of 5,5,8,8-tetramethyl-5,6,7,8-tetrahydronaphthalene with 3-iodobenzoyl chloride (54.6%), followed by Pd-catalyzed vinylation of the iodide with Me acrylate (77%), and hydrolysis of the resultant ester with aqueous NaOH in THF (86%), gave title compound II.

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direct bond; X1 = O, S, SO, SO2, a direct bond; Y = a direct bond, lower alkylene, lower alkylidene; Z = COOH, 5-tetrazolyl, HOCH2, carboxyl derivatized in the form of a pharmaceutically acceptable ester], useful as LTB-4 antagonists, were prepared. Thus, treatment of a solution of (E)-[5-(2-diethylcarbamoyl-1-methylvinyl)-2-(2,6-difluorobenzyloxy)phenyl]acetaldehyde (preparation described) and 2M isobutylene/THF in tBuOH with a solution of NaClO2 and NaH2PO4.H2O in H2O afforded the title compound (E)-II which showed IC50 of 87 nM against LTB-4 binding.

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